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EXAMINER	
CELSA, BENNETT M	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/746,742	ECKERT ET AL.	
	Examiner	Art Unit	
	Bennett Celsa	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-97* is/are pending in the application.

4a) Of the above claim(s) *9,16-37 and 39* is/are withdrawn from consideration.

5)☒ Claim(s) *7 and 8* is/are allowed.

6)☒ Claim(s) *1-6,10-13,38* is/are rejected.

7)☒ Claim(s) *14 and 15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/02;5/02;3/03;9/0*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

Claims 1-97 are currently pending.

Claims 1-8, 10-15 and 38 are under consideration.

Claims 9, 16-37 and 39-97 are withdrawn from consideration as being directed to a nonelected invention.

Election/Restriction

1. Applicant's election of Group I (claims 1-8, 10-15, 38 and 39) in correspondences dated August 29, 2003 and December 11, 2003 and further election of GCN4-pIQI (seq. 25) as the coiled-coil species and Seq. Id. 42 as the gp 41 species, which reads on claims 1-8, 10-15 and 38, is acknowledged. It is noted that the elected species DOES NOT read on claim 39 since seq. Id 21 was not elected. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim Objections

2. Claim 14 is objected to because of the following informalities: In the first line of the claims "HIV gp1" should be --- HIV gp41--- . Appropriate correction is required.

Allowable Subject Matter

3. Claims 7, 8, 14 and 15 are allowable over the prior art of record which fails to disclose or suggest an L/D-peptide, soluble trimeric model of the HIV gp41 hydrophobic pocket which comprises seq. Id. 25 and seq. Id 42.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-6, 10-13 and 38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (lack of written description) .

The present claims are directed to L/ D peptides that comprise:

a. a soluble trimeric form of a coiled-coil and

b. a "sufficient portion of the N-peptide region of HIV gp41 to comprise the amino acid residues which form the pocket of the N-helix coiled-coil of HIV gp41" which "comprises part or all or none of the N-helix coiled-coil pocket of HIV-1 gp41" . See e.g. claims 1 and 38. The resulting peptide must function as "a soluble, trimeric model of the HIV gp41 hydrophobic pocket" (e.g. as a receptor for drug design: see e.g. pages 1-4 of the specification).

The Examples are directed to making and testing a trimeric model of the HIV gp41 hydrophobic pocket which comprises:

a. Specific coiled/coil peptide sequences of GCN4(the yeast transcription activator) e.g. sequences 1 and 25; and

b. Specific HIV gp41 core peptide sequences (e.g. seq. 42).

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Additionally, it is noted that written description is legally distinct from enablement: "Although the two concepts of are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co.*

Although directed to DNA compounds, this holding would be deemed to be applicable to any compound or a generic of compounds; which requires a representative sample of compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the compound or generic(s). In this regard, applicant is further referred to *University of California v. Eli Lilly & Co.*, 119 F.3d

1559, 43 USPQ2d 1398 (Fed. Cir. 1997); "Guidelines for Examination of Patent Applications Under the 35 USC 112, first paragraph, 'Written Description' Requirement" published in 1242 OG 168-178 (January 30, 2001); and Univ. Of Rochester v G. D. Searle and Co. 249 F. Supp. 2d 216 (W.D.N.Y. 2003) affirmed by the CAFC on February 13, 2004 (03-1304) publication pending.

Additionally, Lilly sets forth a two part test for written description:

A description of a genus of cDNA's may be achieved by means of a recitation of: a representative number of cDNA's, defined by nucleotide sequence, falling within the scope of the genus Or

of a recitation of structural features common to the members of the genus.

See *Regents of the University of California v. Eli Lilly & Co.* 119 F.3d 1559 (Fed. Cir. 1997) at 1569.

In the present instance, the claimed peptide's use of functional claim language (e.g. soluble trimeric forms of a coiled coil: "sufficient portion of an N-peptide region ... form the pocket of the N-helix coiled coil" etc.) is devoid of any core peptide structure necessary to produce the desired conformational effect and the ability to mimic receptor action.

Accordingly, the specification discloses only limited examples that are not representative of the claimed genus of peptides which mimic or model the HIV gp41 hydrophobic pocket; nor do the claims recited sufficient structural features which is common to members of the genus sufficient to demonstrate possession of the genus.

6. Claims 1-6, 10-13 and 38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for and L/D peptide which is a soluble trimeric model of the HIV gp41 hydrophobic pocket which comprises an amino acid defined coiled-coil region of GCN4 and an amino acid defined N-peptide region of HIV-1 gp41 as in claims 7, 8,14 and 15, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the presently claimed scope of possible receptor peptide compounds

There are many factors to consider when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any experimentation is "undue". These factors include, but are not limited to:

1. The breadth of the claims.

2. The nature of the invention

3. The state of the prior art;

4. The level of one of ordinary skill

5. The level of predictability in the art;

6. The amount of direction provided by the inventor;

7. The presence or absence of working examples;

8. The quantity of experimentation necessary needed to make or use the invention based on the disclosure;

See :*In re Wands* USPQ 2d 1400 (CAFC 1988):

(1-2) The breadth of the claims and the nature of the invention:

The present claims are directed to L and D peptides that comprise:

a. a soluble trimeric form of a coiled-coil and

b. a "sufficient portion of the N-peptide region of HIV gp41 to comprise the amino acid residues which form the pocket of the N-helix coiled-coil of HIV gp41" which "comprises part or all or none of the N-helix coiled-coil pocket of HIV-1 gp41" . See e.g. claims 1 and 38. The resulting peptide must function as "a soluble, trimeric model of the HIV gp41 hydrophobic pocket" (e.g. as a receptor for drug design: see e.g. pages 1-4 of the specification).

(3 and 5) *The state of the prior art and the level of predictability in the art:*

The specification discloses that "biological activity" of the presently claimed L/D peptides is directed to functioning as a model of the HIV-1 gp41 hydrophobic pocket which is determined by not only primary amino acid sequence structure but primarily as a result of the 3-D conformation of the peptide. See e.g. specification pages 1-5. Thus, in accordance with the present invention, the ability of the claimed L/D peptides to function as an HIV gp 41 receptor to properly bind ligands in a predictable manner is a prerequisite for obtaining "biological activity". However, ligand/receptor binding is stereospecific (e.g conformationally sensitive).(see Rudinger, Peptide Hormones (June 1976: J Parsons editor) pages 1-6; e.g. see page 4; and accordingly, the efficacy of binding of a ligand to a receptor (e.g. enzyme/hormone etc.) to achieve physiological action is determined by the conformation of the ligand and/or its receptor. Thus the different aspects of biological activity cannot be predicted *a priori* but must be

determined on a case to case base through experimental study. The careful design of synthetic analogues and their evaluation in biological systems which permit separate analysis of the various phases of receptor (e.g hormone) action is the best way of obtaining such information. See Rudinger, Peptide Hormones, (June 1976) (J.A. Parsons, editor) 1,5-6. Although the Rudinger article is directed to peptide ligands binding hormone receptors; the conformational sensitivity and unpredictability of receptor/ligand binding is clearly extrapolatable to ligand/receptor interactions generally.

(4) *The level of one of ordinary skill in the art:*

The level of skill would be high, most likely at the Ph.D. level.

(6-7) *The amount of direction provided by the inventor and the existence of working examples.*

The specification and examples are directed to making and testing a trimeric model of the HIV gp41 hydrophobic pocket which comprises:

a. Specific coiled/coil peptide sequences of GCN4(the yeast transcription activator) e.g. sequences 1 and 25; and

b. Specific HIV gp41 core peptide sequences (e.g. seq. 42).

Accordingly, the specification discloses only limited examples that are neither representative of the claimed genus of "receptor" peptides"; nor does the disclosure represent a substantial portion of the claimed genus.

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure:

Accordingly, the undue breadth of possible "biologically active" L/D peptides; the unpredictable effects on bioactivity of subtle changes to the chemical structure and the stereospecificity necessary for receptor/ligand binding, the lack of guidance presented in the specification, the lack of representative examples for both making and use, necessitate the illustration of further examples demonstrating the making and use of a representative sample of HIV gp41 receptor model peptides in order to provide the requisite enablement for the presently claimed invention as broadly claimed.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1, 3, 10, 11 and 38 rejected under 35 U.S.C. 102(b) as being anticipated by Weissenhorn et al. PNAS USA Vol. 94 pages 6065-6069 (June 1997).

Weissenhorn et al. disclose a chimeric fusion protein comprising GCN4-pII coiled coil and the ectodomain-like region of HIV-I gp41 (e.g. an N-peptide region of HIVgp41). The chimeras are taught to be "trimeric-like", "soluble" and "folded-like the ectodomain of viral gp41" and thus meet the conformational and functional limitations of the presently claimed invention (e.g. see abstract; page 6065; page 6067(right column) to page 6068.

10. Claims 1 and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Chan et al. US Pat. No. 6,150,088 (11/2000, filed 4/17/98).

Chan et al. teach peptides which comprise soluble, trimeric forms of a coiled-coil and "a sufficient portion of the N-peptide region of HIV gp41 to comprise the amino acid residues which form the pocket of the N-helical coiled-coil of HIV gp41; the reference peptides comprising N36 (or N51) as the N-peptide and C34 (or C43) as the coiled-coil region. E.g. see abstract; figures, especially figures 1 and 3; columns 1-4. The reference further teaches the use of the reference peptides for "drug design" and screening ligands (e.g. library derived) which bind the hydrophobic pocket of the peptide for generating HIV inhibitors. Eg. See columns 3-7.

11. Claims 1, 2 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. US Pat. No. 6,150,088 (11/2000) and Schumacher et al. US Pat. No. 5,780,221 (7/98: filed 3/96).

Chan et al. teach peptides comprising soluble, trimeric forms of a coiled-coil and "a sufficient portion of the N-peptide region of HIV gp41 to comprise the amino acid residues which form the pocket of the N-helic coiled-coil of HIV gp41 comprising N36 (or N51) ans the N-peptide and C34 (or C43) as the coiled-coil region. E.g. see abstract; figures, especially figures 1 and 3; columns 1-4. The Chan reference further teaches the use of the reference peptides for "drug design" and screening ligands (e.g. library derived) which bind the hydrophobic pocket of the peptide for generating HIV inhibitors. Eg. See columns 3-7.

The Chan et al. reference differs from the presently claimed invention by using a D-peptide of the L-peptide in Chan for use in modeling and/or screening ligands.

However, the Schumacher et al. Patent reference teaches the beneficial use (e.g see col. 5-6 and patent claims) of enantiomeric (e.g. L and D) version of receptors, including HIV receptors (E.g see col. 5) for designing and screening (E.g mirror image phage display) both L and D peptide ligands. See abstract; col. 7; and patent claims 1-14.

Accordingly, one of ordinary skill in the art would be motivated to utilize both the L and D enanatiomeric versions of the Chan et al. HIV gp41 receptor peptides for use in designing and screening prospective D and L peptide ligands for the benefits therein e.g. D-peptides are enzymatically more stable (e.g. see Schumacher col 6).

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to utilize both the L and D enanatiomeric versions of the Chan et al. HIV gp41 receptor peptides e.g. for use in designing and screening prospective D and L peptide ligands for the benefits therein i.e. D-peptides are enzymatically more stable (e.g. see Schumacher col 6).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bennett Celsa whose telephone number is 571-272-0807. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-273-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bennett Celsa
Primary Examiner
Art Unit 1639

BC
March 2, 2004